

Translation

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PCT/EP2003/009105

PATENT COOPERATION TREATY



PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 0000053864	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP2003/009105	International filing date (day/month/year) 18 August 2003 (18.08.2003)	Priority date (day/month/year) 20 August 2002 (20.08.2002)
International Patent Classification (IPC) or national classification and IPC C12N 15/82		
Applicant SUNGENE GMBH & CO. KGAA		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 18 March 2004 (18.03.2004)	Date of completion of this report 10 December 2004 (10.12.2004)
Name and mailing address of the IPEA/EP	Authorized officer
Facsimile No.	Telephone No.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/EP2003/009105

I. Basis of the report

1. With regard to the elements of the international application:*

- ☐ the international application as originally filed
- ☒ the description:
pages 1-43, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____
- ☒ the claims:
pages 1-27, as originally filed
pages _____, as amended (together with any statement under Article 19
pages _____, filed with the demand
pages _____, filed with the letter of _____
- ☒ the drawings:
pages 1/10 - 10/10, as originally filed
pages _____, filed with the demand
pages _____, filed with the letter of _____
- ☒ the sequence listing part of the description:
pages _____, as originally filed
pages _____, filed with the demand
pages 1-18, filed with the letter of 20 December 2003 (20.12.2003)

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in written form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/fig _____

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/EP 03/09105

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	5, 6, 15-17	YES
	Claims	1-4, 7-14, 18-27	NO
Inventive step (IS)	Claims	16	YES
	Claims	1-15, 17-27	NO
Industrial applicability (IA)	Claims	1-27	YES
	Claims		NO

2. Citations and explanations

Reference is made to the following documents:

- D1: WO 99/63055 A (UNIV MARYLAND (US))
9 December 1999 (1999-12-09)
- D2: WO 00/32788 A (HANSENS LAB)
8 June 2000 (2000-06-08)
- D3: WO 98/06862 A (CALGENE INC (US))
19 February 1998 (1998-02-19)
- D4: TIJSTERMAN M ET AL: "THE GENETICS OF RNA
SILENCING", ANNUAL REVIEW OF GENETICS, ANNUAL
REVIEWS INC., PALO ALTO, CA, US, vol. 36, 2002,
pages 489-519, XP009013370 ISSN: 0066-4197
- D5: CARTHEW R W "Gene silencing by double-stranded
RNA", CURRENT OPINION IN CELL BIOLOGY, CURRENT
SCIENCE, LONDON, GB, vol. 13, no. 2,
April 2001 (2001-04), pages 244-248, XP002263320
ISSN: 0955-0674.

1. Novelty and inventive step (PCT Article 33(2) and (3))

1.1 The present application relates to methods for the
production of zeaxanthin in transgenic plants and to

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nucleic acid constructs that reduce the expression of ϵ -cyclase. The use of transgenic plants as ornamental plants and as foodstuffs and animal feed is also claimed.

- 1.2 D1 discloses methods for modulating carotinoid synthesis, according to which methods the suppression of ϵ -cyclase by cosuppression, antisense techniques, ribozyme or "targeted disruption", *inter alia*, is used for the production in plants of β -carotinoids such as zeaxanthin (page 15, line 21 to page 16, line 10; page 17, lines 6-9; page 23, line 30 to page 24, line 7). Reference is also made to the use of the transgenic plants as foodstuffs and food supplements.

Thus, in the light of D1, the subject matter of the current claims 1-4, 7-14 and 20-27 lacks novelty (PCT Article 33(2)). Furthermore, the subject matter of claims 5, 6, 15 and 17-19 is not considered inventive since a person skilled in the art seeking to solve the problem of interest would consider it a routine measure to provide an ϵ -cyclase gene from a further plant or to provide the nucleic acid constructs with a suitable promotor and to express them tissue-specifically.

- 1.3 D2 describes, *inter alia*, methods for the production of β -carotinoids such as zeaxanthin in transgenic plants, preferably in marigold flowers, using antisense techniques to suppress the ϵ -cyclase activity, the endogenous ϵ -cyclase activity being suppressed by the formation of double-stranded ϵ -cyclase ribonucleic acids (page 6, lines 9-12;

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page 6, line 26 to page 7, line 9; page 8, lines 22-34; page 16, line 32 to page 17, line 3; page 23, lines 15-32). The use of the transgenic plants in the production of foodstuffs and animal feed is likewise disclosed (page 12, line 16 to page 13, line 2). The subject matter of claims 1-14 and 18-26 therefore lacks novelty over D2. The cDNA sequence of the ϵ -cyclase of D2 (SEQ ID NO:5) has a sequence identity of 99.9% to the ϵ -cyclase of the present application (SEQ ID NO:4) and therefore, although the nucleic acid construct according to claim 15 is novel over D2 in principle, it cannot be considered inventive since the production of nucleic acid sequences with such a high sequence identity to a known sequence is standard practice for a person skilled in the art.

- 1.4 Document D3, which discloses methods for producing β -carotinoids, also describes the inhibition of ϵ -cyclase by cosuppression or antisense techniques for the production of zeaxanthin (page 11, lines 5-26). The use of these plants or of extracts thereof as foodstuffs, animal feed or food supplements is likewise described in detail (page 3, line 16 to page 4, line 20). In consequence, the subject matter of claims 1-4, 7-14, 18 and 20-27 is not novel over D3 and the subject matter of claims 5, 6, 15, 17 and 19 does not appear to go beyond the modification, in ways that are standard practice for a person skilled in the art, of a method that is known *per se*. Thus, the isolation of an ϵ -cyclase from a further plant and the tissue-specific expression of a corresponding antisense construct is a routine procedure that does not require an inventive step.

- 1.5 D4 and D5 each give a summary of the different methods for using double-stranded ribonucleic acids to reduce gene activity. Reference is made to specific embodiments, for example the use of inverted repeats.

2. Further observations

In claims 2, 3, 12-14 and 22, the expression "a part" is vague and unclear, being defined in very general terms (page 6, lines 18-23), and leaves the reader uncertain as to the meaning of the technical feature in question (for example this definition encompasses the sequence of two base pairs). As a result, the subject matter of said claim is not clearly defined (PCT Article 6).